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Physiology and clinical observation show that water plays an active and very special part in the nutrition of infants. The variation in the water content of the organism at different stages of existence: 97.5% for the six-week embryo, 73.9% for the mature foetus, 69% for the newborn baby, 63-58% for the adult; the difference in water requirements: 150 grams per kilo for a nursing infant, 35-40 grams per kilo for an adult; the physiological variation in hydremia (Lederer): from 80% at birth it falls to 71.8% in 18 hours, then returns slowly to a maximum of about 81%, reached only toward the fourth month, and, finally, falls very slowly but continuously, up to the end of the first year. All these data go to show that, physiologically, in early infancy the water metabolism has a special character, in keeping with the requirements of rapid growth. Accordingly, it is not surprising that all ailments of any importance, capable of affecting the general nutrition of young children, should disturb the water balance of the organism and find external expression in one of the following syndromes: dehydration, pathological hyperhydration, disturbance of the organism's fluid distribution mechanism, and the binding of water in the tissues (hydrolabile paratropy).

In fact, when one comes to make a general study of one of these states, one becomes rapidly convinced that the water problem is one that affects all aspects of the pathology of the nursing infant; thus, the problem appears as one of central importance, closely linked with a whole series of special problems that are at best imperfectly understood.

At the French Congress of Medicine 1927 the physiopathology of edemas was the subject of papers and discussions of the highest interest, as a result of which it became clear that a variety of factors was involved. These include a circulatory factor (circulatory regime, variation of capillary permeability, vasomotor effects), a renal factor, a humoral factor (modification of protein levels in blood serum, albumin/globulin ratio, osmotic pressure of proteins), a histological factor (variation of the mineral balance of the organism, alteration in the ionic acidity of the fluids and tissues, in the lipocyte factor, displacement of isoelectric points of proteins). These are the new data that the biologists have produced with a view to solving the water problem by the increasingly refined

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methods used in physicochemical investigations of the physiology of the tissues. These various factors that have been identified by experimental analysis sometimes act in isolation and, in general pathology, we distinguish between cardiac edemas, renal edemas, angio-neurotic edemas, and edemas due to nutritional disorders, but it would no doubt be illusory to carry these distinctions too far, and in actual cases, which are never simple, one rather gets the impression that the various disordered mechanisms combine and interfere with each other.

In the special case of early infancy, the edemas due to nutritional disorders are by far the most important. It is precisely in connection with edemas of this type that the pathogenic uncertainty is greatest, so much so that a quick review of the subject soon reveals that there is not one but several modalities of nutritional disorder leading to edema. Being unable to classify the edemas of the nursing infant on a physiopathological basis, in the paper that I submitted to the Congress of Pediatrics, I attempted to assemble the facts in accordance with their clinical etiology.

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Disregarding the phenomena that can be simply attributed to obvious congenital malformation of the heart, the portal system, the urogenital apparatus, compression of the inferior vena cava, etc., edemas fall neatly into three groups:

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1. syphilitic edemas;
2. nonsyphilitic edemas of the newborn;
3. so-called idiopathic edemas, i.e. those in connection with which the possibility of an inflammatory impairment of the kidneys can be dismissed.

Actually, it would be advisable to add to these the very common physiological pubic and genital edema of the newborn and cases of idiopathic chronic genital edema (Friedjung), and genito-pubic scleredema of the newborn (Woringer). Woringer considers that this is a rare complaint, clearly distinct from physiological edema, and it might be desirable to open a new chapter with this heading in the highly specialized pathology of the newborn.

Syphilitic edemas. In connection with syphilitic anasarca, I may not have paid sufficient attention to this highly important

variety in my paper. It seems to me that, at least in France, the role of conceptive syphilis has not been underestimated. Lereboullet and Lelong, Lemaire and Mlle. Desbrousses have very properly taken up the question and stressed the wide range of facts which, in early infancy, are directly traceable to syphilis. Apart from the hepatonephritis of malignant hereditary syphilis, there are less severe, curable syphilitic anasarcas, in which the kidneys are not always affected; and it is noteworthy that in early infancy syphilis produces edemas by different mechanisms: kidney attack dominant, tissue changes only. Finkelstein draws attention to this expressly. The appearance of this anasarca is more or less precocious; sometimes the disease precedes birth (congenital anasarca with dropsy of the amnion); sometimes it develops during the first months. It may also be slower in appearing.

The point on which we laid stress, in connection with congenital anasarcas, is the contradiction between the theory, in accordance with which French obstetricians and pediatricists agree in attributing to syphilis the great majority of cases of congenital anasarca, and the opposite tendency that prevails abroad. The research of Schridde, von Jaschke, N. B. Capon, Kratzeisen, and Ballhorn leads to the conclusion that in most cases the trouble has nothing to do with syphilis and, under the name "hepatic erythroblastosis with congenital anasarca," they establish a special nosological type defined by abnormal centers of hematopoiesis in various organs, in particular the liver. We thought it necessary to attach some formal reservations to this interpretation. Ribadeau-Dumas, who formerly studied, with Courcoux and Pater, the revivescence of hematopoietic centers in heredosyphilitic livers, and, experimentally with Rist, the infectious myeloid-type granulomas of spirillosis in hens, has produced a more decisive critique of hepatic erythroblastosis.

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Nonsyphilitic edemas of the newborn. However, though conceptive syphilis must be accorded a very large share in the etiology of edemas in infants, it should not be regarded as the exclusive factor. It is common to observe severe edemas, true generalized anasarcas, in the newborn that are not syphilitic and reveal no trace of inflammatory impairment of the kidneys. Here we can distinguish two groups of opposing facts, particularly in relation to prognosis.

1. Anasarca of feeble, prematurely born infants who have not been properly protected from the cold. Inert, drowsy, cyanotic, their pulse weak and slow, these children grow cold. The disturbed thermal regulation (Hutinel), and insufficiency of hematosi (Marfan)

lead to paralytic vasodilatation, cyanosis, and edema. These children rapidly succumb. Sometimes the fatal outcome is delayed; they develop cachexia, the edematous tissues become hard, and edema becomes sclerema.

2. However, apart from debility, the tendency to grow cold, and any acute or syphilitic infection, the newborn are subject to anasarcas, the origin of which is still very obscure. These develop in a few hours in the days following birth, in infants in good general condition, even nursing infants. The prognosis is not particularly serious, especially if the infant is receiving its mother's milk, and the absence of hypothermia is a good sign.

These cases, which are not very common, are of very great general interest. In our opinion, their interpretation depends on the introduction of a functional disturbance of the mechanism regulating the water and mineral salt metabolism. Apart from any obstetrical accident, the passage from an intra-uterine to an extra-uterine existence is a critical period for the organism of the newborn, since it suddenly experiences a profound disturbance in the mode of functioning of its organs: acquisition of the pulmonary respiratory function, initiation of gastrointestinal digestion, transition from an environment at a constant temperature to one in which the temperature varies, whence the need for active thermal regulation. There are many things, which may or may not be considered as normal physiological reactions, that testify to the more or less considerable difficulty of this adaptation: the thermal irregularities of the first few days, temporary albuminuria, physiological icterus, etc. Now, in the particular case of the problem of water and edemas of the newborn, it is necessary to take into account various factors closely connected with the physiological traumatism of birth.

Birth is followed by an initial fall in weight, a sudden dehydration of the fluids and tissues (Lederer), and rapid growth -- this is a general law of biology -- depends entirely on an intense fixation of water. Above all, the organism of the newborn is greedy for water. In the infant, the kidneys show signs of imperfect functioning and a real difficulty in osmo-regulation (Nobecourt and Maillet). The addition to the diet of small quantities of sodium chloride leads to the retention of water and an increase in weight. This apparent gain, however, is only temporary, and after some time the organism adapts itself by an increase in diuresis, and if the administration of chloride continues, not only does the increase in weight cease but part of the water originally retained is eliminated, and the organism restores a physiological balance between what it takes in, what it eliminates and the fixed quantities (Nobecourt, Finkelstein, L. F. Meyer).

Given temporary functional inhibitions disturbing the regular

mechanism of the circulation of the blood by way of vasomotor effects, the functioning of the kidneys as a secretory organ regulating the balance of water and salts, physicochemical changes in the tissue albumins, and the failure of these different mechanisms to work harmoniously and in coordination, it is easy to see how retention of water and edemas can develop, particularly in the presence of debility, or when the infant suffers from a rather serious or prolonged nutritional disorder.

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So-called idiopathic edemas. Edemas not connected with nephritis affect children who are in other respects distinctly pathological. The ailments that lead to or accompany the edema are most diverse. They do, however, have something in common. They produce an intense and often lasting change in the general condition. They chiefly comprise nutritional disorders, and it is reasonable to assume that in an organism in the process of rapid growth the entire constitution of the tissues and the physiological properties of the cells are affected. The edema is, at one and the same time, a consequence of these nutritional disorders and one of the modalities of the profound change in the constitution of the tissues.

From the etiological point of view, these nutritional disorders can be classified under four distinct headings:

1. Edemas and states of undernutrition.
2. Edemas and constitutional states.
3. Nutritional edemas.
4. Edemas and infections.

1. Edemas and states of undernutrition. Edema is common in children suffering from chronic and progressive undernutrition. The hyperhydration appears in the weight charts, and rapid and excessive gains in weight in hypothreptics and athreptics are by no means a favorable symptom.

General analyses of the body and the different tissues of athreptics reveal an increase in the proportion of water. Finkelstein considers edema to be a characteristic symptom of the stage of decomposition, and Ribadeau-Dumas, with his pupils Fouet, J. Meyer, J. Debray, and Mlle. Tisserand, has established that in athreptics, rather than an infection or a passive congestion, pneumopathy is an edema expressive of an excessive hydration of the child's organism.

In the course of athrepsia, the blood becomes poor in proteins and mineral salts (Mariott, Utheim); on the other hand, in severe cases of acute, choleriform undernutrition, dehydration and anhydremia

are at a maximum. Without dwelling on the important clinical differences between athrepsia and choleriform intoxication -- states which Parrot nevertheless confuses -- it is possible to draw attention to the contradictory behavior of the organism with respect to liquids [resorption tests on subcutaneously injected serums (Ribadeau-Dumas); variations in the level of hydremia after digestive absorption of the same quantity of water (Rominger)]; and yet edema is not rare in choleraic infants. True, it is late in appearing, not before the fourth or fifth day, often after attempts at rehydration by means of massive injections of serum. But the coexistence of subcutaneous edema and obvious dehydration of the tissues is an extremely striking indication of something seriously wrong with the water metabolism. The thought of this organism, needing water so badly yet utilizing it so awkwardly that it stores an unused portion in the interstitial spaces of the cellular tissue, is enough to provoke a certain scepticism in relation to the proposed methods of rehydrating choleraics by means of hypodermic injections of isotonic solutions. The thing is not merely to supply the organism with water, but to supply it with water in a form that it can use. Marfan states that a choleraic cannot be rehydrated except by giving him water through the natural channel, the digestive tract.

In the toxic syndrome, the usual bond between water and the tissues is temporarily broken. Besides, there is no contradiction, as might appear, between cellular dehydration and interstitial edema. In accordance with a working hypothesis advanced by Ambard, we can visualize a sudden change in the physicochemical state of the tissue albumins -- a change in the isoelectric point of the albumins -- freeing a certain amount of water, which is partly eliminated through the intestines and the lungs, partly expelled into the interstitial spaces, where it accumulates, unused and extraneous to the organism. As Ambard recalls, in the physiopathology of edemas we must not forget the case of the patient who went to sleep one evening feeling well and awoke the next morning puffy and edematous, without having ingested either water or salt in the meantime. In this case we are faced not with an imbalance between the intake and elimination of water, but with a change in the distribution of the water actually present in the organism at the time.

2. Edemas and constitutional states. Edema with its degrees of hyperhydration is a common syndrome accompanying certain diathetic states, in harmony with the very constitution of the child born with a congenital predisposition to certain nutritional disorders: dysosmotic constitution (Lesage), dropsical constitution (Czerny), hydrolabile paratophy (Finkelstein). It is best seen in certain eczemas, erythroderma desquamativum, tetanus, and the anemias of early infancy. The superb studies of Ribadeau-Dumas, with R. Mathieu

and Max and Erna Levy, on the humoral syndrome of the exzematous (increased water content of the serum, hypoproteinemia, inversion of the albumin/globulin ratio) provide an objective basis for the concept, previously rather vague, of diathetic eczema and lead these authors to make an interesting comparison between eczema and lipoid nephrosis, a comparison previously suggested from the clinical angle by Stolte and Knauer.

3. Nutritional edemas. The above facts clearly indicate how severe and prolonged nutritional disorders can create a predisposition to edema, a state fairly close to one of congenital, constitutional origin. But among those so predisposed, edema very often occurs as a result of nutritional or therapeutic factors. Even more strange, by means of certain diets or certain therapeutic techniques, one can produce in babies, almost at will, and independently of any truly pathological factor, a retention of water that turns more or less rapidly, depending on the constitutional state, into a real edema. It is of the greatest importance for the pediatricist to know how the different constituents of the diet effect the retention, elimination and fixation of water by the organism. The different constituents of a diet (salts, carbohydrates, albumins, fats, vitamins) may act individually if they are present in excess, deficient or unbalanced.

Four types of diets are hydropigenous: hypermineralized diets, carbohydrate diets, unbalanced fat- and protein-deficient diets, generally deficient diets.

This is shown by many clinical and experimental data.

The hydropigenous effect of sea salt has been solidly established since the work of Achard, Widal, Lemierre and Javal. In pediatry, it has often been confirmed. It is enough to recall the edemas frequently observed in treating digestive troubles with a bouillon of salty vegetables, decoctions of cereals, Heim and John's solution, injections of physiological serum, sea water, and Ringer's mixture. These chloride edemas develop very rapidly and, conversely, subside in a few days, when the supply of chloride is cut off. Thus, as L. F. Meyer remarks, they differ from flour edemas, which develop slowly and are equally slow to disappear. However, certain objections have been raised against the theory of hydropigenous chloride retention, at least as a general, exclusive theory. Freunds, Czerny, Keller, Schloss, Klose, and Jundell do not admit that the two problems: that of water and that of salt are always connected. Lederer considers them to be distinct. This is a difficult and controversial question, but it appears that the following conclusions may be drawn:

1. In the infant, and especially in the feeble infant, the constitutionally predisposed or the hypothreptic, progressive chlorination of the organism easily leads to the retention of water and edema.

The infant organism easily falls into a state of chloride retention, and if this disorder is not more commonly observed, it is doubtless, as Variot suggests, because in reality the diet of infants is only very weakly chlorinated.

2. A general theory of edemas that confined itself to the consideration of chloride edemas would certainly fail to take into account all the facts and perhaps even the important ones.

Perhaps, moreover, it would be preferable to broaden the problem and consider not the chloride balance alone, but the mineral balance of the organism as a whole. This is the point of view adopted by Barbier, who, basing himself on the experiments of Le Play, has described as accidents of hypermineralization the florid atrophy of infiltrated, oliguric, overnourished hypotrophics, with a poor tolerance of cow's milk.

When a child is given food rich in carbohydrates, a farinaceous diet, it is common to observe a simultaneous sharp increase in weight and a marked decrease in diuresis.

As is well known, especially since the work of Czerny's school, children kept on a farinaceous diet often, at least in the early stages, have a florid appearance, satisfactory weight, and very good turgor. A more or less severe nutritional disorder was the reason for their being put on a floury diet. Later on, various troubles may develop: muscular hypertonia (Rietschel), atrophy, and especially edemas. But without going as far as the edema stage, there is one point particularly worth noting: this is the instability of the gain in weight. Broad variations in weight, a wavering progress, and sudden collapse indicate that the total weight includes a mass of water superadded to the tissues. This hyperhydration appears most clearly when these big, florid, but often pale babies are put on a new diet and given fresh, more varied food, rich in albumin and fats.

Very often the transformation in the general state and the benefits of this diet are clearly apparent; however, the first thing to be observed is a loss of weight and, if no change is made in the new diet, it is only after several days, and often even after several weeks, that a gain in weight gradually reappears, the stage of growth being preceded by a stage of restoration. In more serious cases, severe edemas characterize the edematous form of flour dystrophy.

Mouriquand and Rabat, Ribadeau-Dumas, R. Mathieu, and Max Levy have described some typical examples.

These cases remain very complex from the physiopathological point of view, for there is not only an excessive consumption of carbohydrates, but an unbalanced and deficient diet. In the presence of these high-carbohydrate, low-chloride diets, there is no retention of salt parallel with the retention of water (L.-F. Meyer). Keller notes that if a large amount of salt is then administered, the

organism retains a large part of it, as if it were in a state of deficit, with a chloride appetite (Cl. Hunger). This is in line with the findings of Salge, who observed a fall in chloremia, but only in very young children whose nutrition had been seriously affected.

These clinical facts relating to the hydropigenous action of exclusively carbohydrate diets are also strongly supported by the experimental data (Soxhlet, Weigert, Voit, Lederer, etc.).

Edemas and deficient diets. Diet deficiencies certainly play an important part in the pathogeny of edemas. Experimentally and clinically, the results of being deprived of the liposoluble vitamin A (hikan, xerophthalmia) and the antineuritic vitamin (beri-beri) lead to edema.

In France, cases of this kind are relatively rare, but they should not be forgotten when it comes to analyzing the hydropigenous effects of an exclusively carbohydrate, deficient, and unbalanced diet. In connection with nutritional anasarcas, Ribadeau-Dumas, R. Mathieu and Max Levy try not only to cover and make good the protein deficiency, but to supply a great abundance of vitamins of all kinds. This is also one of the objects of R. Hamburger and B. Epstein in instituting their milkless diets in early infancy.

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4. Edemas and infections. Our etiological study would be incomplete, if we failed to mention the insidious part played by infections, even in the complete absence of nephritis. In florid, infiltrated babies, infections result in an often rapid fall in weight; during convalescence, there follows a period of intense rehydration which may even develop into edema. Thus, Pirket has drawn attention to post-infection edemas which precede the appearance of albuminuria. Czerny and Keller are inclined to consider that this is not the work of nephritis, but rather that the albuminuria depends on the plasma disorders responsible for the edema.

In early infancy, a certain number of infectious diseases lead to edema without nephritis: scarlatina, pneumonia, measles, chicken pox. Barbier has observed edemas fairly frequently in young tuberculosis patients.

In connection with post-infection edemas of the nursing infant, it is difficult to define clearly the part played by the infectious disease and to isolate it from the nutritional factors, digestive disorders, and inanition.

The role of the infection is decidedly obscure; its relations with the processes of hydration are comparable with those it has with the appearance of the symptoms of tetanus.

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The above classification of the etiological forms of edemas of the nursing infant, though convenient for the purposes of this paper, is really quite artificial. In the clinic, cases are rarely straightforward and, for example, certain cases classified as nutritional edemas could legitimately be described as constitutional edemas. Children are not all equal when they are born and do not respond in the same way to hydropigenous factors.

The hydropigenous effect of salt is well established, but it does not manifest itself in exactly the same way in all infants that ingest the same saline solution. "If the same dose of salt causes pitting edema in one, a retention of water deducible only from the weight in another, and has no effect on a third, there must be some other factor apart from nutrition at work, a factor which must depend on the particular tendency of each child to become edematous. This individual factor may be congenital or acquired (L.-F. Meyer)." /93

Barbier places florid atrophy by hypermineralization within a very broad frame. In this connection he uses the term "cow's milk pathology." But to assume a cow's milk pathology when everyday experience brings one continually in contact with fine children that thrive on such a diet is surely to recognize that those suffering from florid atrophy have in their organism a constitutional defect that prevents them from adapting themselves to a cow's milk diet. This, moreover, is the conclusion that Barbier himself has developed on numerous occasions.

The younger the organism, the more dependent it is on external factors, including nutrition, and the more profound the changes in the composition of the fluids and tissues imposed by variations of diet (Weigert, Lederer). But here, too, the constitution plays a part, since the length of the period during which the young child is heavily dependent on the outside world varies with the individual (Salge).

In numerous animal experiments that demonstrate the hydrating effect of hyperchlorurated, high-carbohydrate, fat- and protein-deficient diets, it has not been possible until recently to make adequate allowance for the vitamin deficiencies that do so much to complicate matters.

It is very interesting to compare nutritional edemas with famine and war edemas at all ages. This is a valid comparison and Forest was right to draw attention to it and lay special stress on the part played by diet deficiencies and the therapeutic conclusions that may be drawn. Nevertheless, the seriousness of these states should not be underestimated. Individuals, adults or children, who have suffered nutritional anasarca without nephritis and do not appear to have any deepseated, irreparable, and possibly fatal visceral lesion, are actually very delicate and vulnerable. The diet should be very carefully controlled, since the recuperation

stage is very protracted. By rebalancing the diet, enriching it in all kinds of vitamins, the edema can be reduced fairly rapidly, but the game is not yet won and too often a more or less sudden death due to cardiac collapse shatters all hope, at a point where one felt justified in considering the patient well on the way to recovery. This notion, which is of great practical importance, should not be forgotten by the pediatricists who treat edematous infants. Lederer has clearly underlined the danger. When a child nourished exclusively on farinaceous foods and suffering from an anasarca is immediately returned to a balanced, complete diet, the edema may be very quickly cured, but the profound disturbance of the tissue metabolism is not corrected for a long time, and in certain circumstances, even on mother's milk, a sudden collapse may occur. Lederer recommends a slow, gradual method, in which the various nutritional insufficiencies and deficiencies are pared away, without an abrupt and massive restriction of the carbohydrate ration. This prolongs the cure, but provides better protection from accidents due to imbalance and intolerance.

In early infancy edemas are of very frequent occurrence, particularly in the younger children and those whose general state is more seriously affected. The cardiac and renal changes that predominate in the older child and the adult are in this case relegated to the background. The edemas of early infancy are primarily connected with the general metabolism and the nutrition. The nutritional factors that make so profound and lasting an impression on the organism in the process of active growth have an obvious effect. Certain serious dietary deficiencies lead to profound disturbances of the tissue metabolism, to the pathological retention of water, and to edema. But, however active these factors may be, they do not produce their full effect unless they act on an organism predisposed to succumb to them.

This predisposition may be congenital, as one learns from clinical observations. It may also be acquired as a result of various morbid conditions.

The general body of facts observed in the infants' clinic supports the hypotheses that relate the problem of the pathological retention of water to nutritional disorders.

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